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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/885,259	02/23/2001	Madhav N. Devalaraja	PC18174A	3713

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	PAPER NUMBER
1644	15

DATE MAILED: 07/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/885,259	Applicant(s) DEVALARAJA ET AL.	
	Examiner Michail A Belyavskyi	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12, 14 , 31, 33-34, 36-37, 39, 41-42 and 44 - 50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12, 14 , 31, 33-34, 36-37, 39, 41-42 and 44 - 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 06/16/03 (Paper No. 13), is acknowledged.

Claims 12, 14 , 31, 33-34, 36-37, 39, 41-42 and 44 - 50 are pending.

In view of the amendment, filed 6/12/02(Paper No. 13), the following rejections remain

2. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the same reasons set forth in the previous Office Action, Paper No: 10, mailed 1/28/03

Applicant's arguments, filed 06/16/03 (Paper No. 13), have been fully considered, but have not been found convincing.

Applicant asserts that the word "psoriasis " was deleted and the word "asthma" was inserted. However, it is noted the amended claim 42 still recited " ...treat said psoriasis..".

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 12, 14 , 31, 33-34, 36-37, 39, 41-42 and 44 - 50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: 1) a method for screening for an inhibitors of a CSF and mCSF in vitro assays based on inhibition of chemoattraction and/or accumulation and /or activation of leukocytes by CSF and;2) in vivo recruitment assay response to IL-8, using rabbit as animal model, does not reasonably provide **enablement** for: 1) a method of treating inflammation, such as sepsis, or osteoporosis an autoimmune disease or

atherosclerosis, comprising administering to a mammal a therapeutically effective amount of an antibody to M-CSF, claimed in Claims 12 and 14, or 2) a method of treating inflammation, such as psoriasis or asthma, comprising administering to a mammal a therapeutically effective amount of an antibody to M-CSF, claimed in Claims 31, 37 and 42 or 3) a method of treating rheumatoid arthritis in a mammal comprising administering an antibody to M-CSF, claimed in Claims 34 and 50. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action, Paper No: 10, mailed 1/28/03

Applicant's arguments, filed 06/16/03 (Paper No. 13), have been fully considered, but have not been found convincing.

Applicant asserts that: (i) One of the skill in the art can make antibody against virtually any protein, thus can practice the claimed methods of using M-CSF antibodies without undue experimentation; (ii) it is well within the purview of the ordinary skilled scientist to determine a therapeutically effective amount of an anti-M-CSF antibody and to determine if a subject is benefiting from the therapy.

Contrary to Applicant's assertion, the issue raised in the previous Office Action was not about ability of one skill in the art to make antibody or determine a therapeutically effective amount of an anti-M-CSF antibody.

In the previous Office Action it was stated that the specification only discloses detailed *in vitro* chemotaxis assay , calcium flux assay and binding assay (Example 1 of the Specification as filed), a protocol screening assay for G-CSF receptor antagonists (Example 2 of the Specification as filed) and a protocol screening assays for inhibitors of the synergistic effect of M-CSF on a chemokine-induced, monocytes-mediated inflammation, based on directly measuring activation of human monocytes (Example 3 of the Specification as filed). The specification does not adequately teach how to effectively treat inflammation, including sepsis, rheumatoid arthritis, asthma and psoriasis, by administering an effective amount of an antibody to M-CSF. Moreover, no animals were used as model system to effectively treat inflammation in a subject, comprising administering to the subject an effective amount of an antibody to M-CSF. Since there is no animal model system in the specification to effectively treat inflammation by administering to a mammal a therapeutically effective amount of an antibody to M-CSF, it is unpredictable how to correlate *in vitro* results with *in vivo* use. The references provided by Applicant , for example Williams et al (IDS) teach the use of neutralizing anti-TNF-alpha monoclonal antibody can ameliorate arthritis only in mice model with type II collagen –induced arthritis. However, Feldman et al (IDS) teach that "while it is not difficult to study the pathogenesis of animal models of disease, there are multiple constraints on analyses of the pathogenesis of human disease, leading to interesting dilemmas such as how much can we rely on and extrapolate from animal models in disease". Feldman et al . further teach that in a chronic immune-driven inflammatory response there are a number of pathways that become

engaged and effective therapy in immune inflammatory diseases such as rheumatoid arthritis, will come from therapy aimed at several points in the disease pathway. Moreover, Aoki et al (US Patent 5,470,578) teach that the cause of a chronic multiple inflammatory disease, rheumatoid arthritis, is still unknown and no reliable treatment of the disease has been established (see entire document, column 1, lines 55-60 in particular). Since the method of treating inflammation, by administering to a mammal a therapeutically effective amount of an antibody to M-CSF can be species- and model-dependent (seeVan Noort et al. International Review of Cytology, 1998, v.178, pages 127-204, Table III in particular) , it is not clear that reliance on the *in vitro* studies accurately reflects the relative mammal and human efficacy of the claimed therapeutic strategy. The specification does not teach how to extrapolate data obtained from *in vitro* studies to the development of effective *in vivo* mammalian including human therapeutic treatment, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of a method of treating inflammation, including sepsis, rheumatoid arthritis, asthma and psoriasis by administering to a mammal a therapeutically effective amount of an antibody to M-CSF . Moreover, Applicant himself acknowledge that the ability of CSF to synergistically enhance the chemoattractant effects of chemokines on recruitment of leukocytes to sites of inflammation was unexpected (page 4, line 8 of the Specification as filed) . As such, the invention must be considered unpredictable.

The specification does not provide sufficient teaching as to how it can be assessed that treating inflammation in a subject, including sepsis, rheumatoid arthritis, asthma and psoriasis was achieved after the administration of a therapeutically effective amount of an antibody to M-CSF Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of treating inflammation in a subject, including sepsis, rheumatoid arthritis, asthma and psoriasis, comprising administering an effective amount of a therapeutically effective amount of an antibody to M-CSF in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

6. No claim allowed

7. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
July 28, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
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